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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,968	02/20/2004	Kevin J. Williams	W1107/20009	9607

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,968	WILLIAMS, KEVIN J.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/03/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *241,242,244,245,248-250,252,253,256 and 265-370* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *241,242,244,245,248-250,252,253,256 and 265-370* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment and Arguments

1. Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 265-370 are pending.

Claims 317-370 have been added.

Claims 249, 276 and 312 have been amended.

Claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 265-370 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection

Claim Objections

3. Claim 274 is no longer objected to because the claim ends with a period.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claims 276 and 312 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention is withdrawn because these claims now recite amino acid residues and corresponding position numbers.

5. The rejection of claim 309 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn because of Applicant's arguments submitted September 3, 2009, see page 34.

Double Patenting

6. The provisional rejection of claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 163, 164, 166-168 and184-193 of copending Application No. 10/419,462 (filed February 20, 2004) is withdrawn in view of the arguments presented in the Remarks submitted September 3, 2009, see page 36.

Maintained and New Grounds of Rejection

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The **NEW MATTER REJECTION** of claims 309-316 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicant mischaracterizes the Examiner's rejection by stating "...the rejection [means] the term "antibody", not "binding agent", should be used in the claim.", see Remarks submitted September 3, 2009, bridging paragraph of pages 31 and 32. Applicant points out support can be found in the specification, page 18, lines 2-6. Applicant directs the Exmainer's attention to the meaning of epitope and its relationship to a binding agent. The Examiner has carefully reviewed Applicant's Remarks and those sections of Applicant's disclosure and finds these arguments unpersuasive.

Applicant's claims 309-316 continue to introduce new matter. Simply put Applicant's claims read on quantifying thrombospondin and/or thrombospondin fragments. Those sections of the specification that Applicant's rely upon for support do not. Page 18, lines 7-13 of the disclosure read on quantifying thrombospondin/thrombospondin

fragments *based on detection of epitopes*. The claims and the specification read on two different manners of quantifying thrombospondin/thrombospondin fragments. The Examiner notes in Applicant's disclosure the use of binding agents in detecting epitopes, however that is not set forth in the claims. The pending claims are broader than what is set forth in the specification. Applicant continues to not have support for these new claims and should delete the new matter or pointedly express in the specification by page and line number where support is found.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The rejection of claims 241, 242, 244, 245, 248-253, 256, 265-316 and new claims 317-370 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and made.

a. Claims 241, 249, 276, 289, 297, 303 and 309 are vague and indefinite because these claims recite an individual's plasma level of thrombospondin fragment or fragments is used in a diagnosis, wherein

the plasma level is greater and if so it is implicative of the individual has a neoplastic disease.

Applicant notes with the phrase "greater than" being a part of the claims the comparison step is implicit in the claims and notes two of the dependent claims clarify the comparison between two individuals or the same individuals at successive time points, see Remarks, bridging paragraph on pages 32 and 33. These points of view have been carefully considered, but found unpersuasive.

However, there is no "greater than" phrase listed in the independent claims and while comparison steps may be listed in dependent claims this clarity should be clear in the independent claims from which dependent claims stem. It continues to not be clear what plasma level of thrombospondin denotes neoplastic disease and what this level is compared to and what population this greater than quantity should be compared. The metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. The rejection of claims 241, 245, 248, 249, 253, 256 and 265-276 under 35 U.S.C. 102(b) as being anticipated by Jackowski et al./ U.S. Patent application publication number 2003/0119074 A1 (December 20, 2001) is maintained.

Applicant asserts "...Jackowski does not disclose an assay directed at the diagnosis of neoplastic disease" and Jackowski's invention is directed toward Alzheimer's disease, see Remarks submitted September 3, 2009, page 35. Applicant's points of view have been carefully considered, but found unpersuasive.

Applicant is reminded that there claims read on two particular method steps, wherein an individual's plasma level of thrombospondin fragment/fragments is measured and using the said measurement to

decide whether or not a greater plasma level is implicative of a neoplastic disease diagnosis. Remiss from the claims are the patient population measured and the populations the plasma levels are compared to. Jackowski reads on these two method steps hence the rejection is maintained and reiterated below.

Jackowski disloses a method of detecting immunological fragments of thrombospondin with an antibody or binding partner in a plasma sample, see abstract; page 3, section 0029; page 5, section 0065. Absent evidence to the contrary the molecular weight of said fragment or any of said fragments not exceeding 140 kDa, the molecular weight of said fragment or fragments being at least 20 kDa, wherein the size in kDa is that detemained by gel electrophoresis after disulfide bond reduction, and wherein the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat.

13. The rejection of claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 under 35 U.S.C. 102(e) as being anticipated by McCarthy/ U.S. Patent Application Publication number 2003/0166017 A1 (filed November 9, 2001) is maintained.

Applicant asserts "...McCarthy does not disclose an assay directed at the diagnosis of neoplastic disease" and McCarthy's invention is directed toward cardiovascular disease, see Remarks submitted September 3, 2009, page 35. Applicant's points of view have been carefully considered, but found unpersuasive.

Applicant is reminded that there claims read on two particular method steps, wherein an individual's plasma level of thrombospondin fragment/fragments is measured and using the said measurement to decide whether or not a greater plasma level is implicative of a neoplastic disease diagnosis. Remiss from the claims are the patient population measured and the populations the plasma levels are compared to. McCarthy reads on these two method steps hence the rejection is maintained and reiterated below.

McCarthy discloses a method of assessing the level of a TSP fragment in plasma using an antibody or ligand, which reads on Applicant's active step of measuring an individual's plasma level of thrombospondin fragments, see page 2, section 0017; page 4, section 0059; page 5, section 0061; page 8, section 0095; page 9, sections

0096, 0099 and 0100; and page 10, section 0103. Moreover, the level of a TSP fragment or marker may be comparatively assessed, whereby the 'normal' level of TSP marker is determined and compared to a patient sample, see page 5, section 0066. Absent evidence to the contrary the molecular weight of said fragment or any of said fragments not exceeding 140 kDa, the molecular weight of said fragment or fragments being at least 20 kDa, wherein the size in kDa is that detemained by gel electrophoresis after disulfide bond reduction, and wherein the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The rejection of claims 241, 242, 244, 245, 248-250, 252, 253, 256 and 256-316 under 35 U.S.C. 103(a) as being unpatentable over WO 98/07035 (published 19 February 1998), and further in view of McCarthy/ U.S. Patent Application Publication number 2003/0166017 A1 (filed November 9, 2001)is maintained.

Applicant cites the improper statute, 102(e) when traversing the instant rejection. Applicant asserts neither the WO document or McCarthy teaches an assay directed toward the diagnosis of neoplastic disease, see Remarks, page 36. Applicant's points of view have been carefully considered, but found unpersuasive.

Applicant is reminded that there claims read on two particular method steps, wherein an individual's plasma level of thrombospondin fragment/fragments is measured and using the said measurement to decide whether or not a greater plasma level is implicative of a neoplastic disease diagnosis. Remiss from the claims are the patient population measured and the populations the plasma levels are compared to. The

deficiences of the WO document are addressed and taught in McCarthy hence the rejection is maintained and reiterated below.

The WO document teaches antibodies that detect thrombospondin fragments (collectively referred to as "ADP") in a body fluid, see abstract; bridging paragraph of pages 11 and 12. The antibodies cross-react with 67-80 kDa and 20kDa fragments of thrombospondin-1, see page 7, 2nd paragraph; and page 9, 1st full paragraph. Absent evidence to the contrary the fragment or each of said fragments comprises a portion of thromobospondin selected from the group consisting of a collagen type V binding domain, and a domain or a part thereof within the protease-resistant core of thrombospondin, said domain being selected from the group consisting of a domain of inter-chain disulfide bonds, an oligomerization domain, a procollagen-like domain, a type 1 repeat, a type 2 repeat, and a type 3 repeat. The WO document does not teach the comparison of amounts of TSP fragment plasma levels between two individuals.

However, McCarthy teach a method of assessing the level of a TSP fragment in plasma using an antibody or ligand, which reads on Applicant's active step of measuring an individual's plasma level of thrombospondin fragments, see page 2, section 0017; page 4, section 0059; page 5, section 0061; page 8, section 0095; page 9, sections 0096, 0099 and 0100; and page 10, section 0103. Moreover, the level of

a TSP fragment or marker may be comparatively assessed, whereby the 'normal' level of TSP marker is determined and compared to a patient sample, see page 5, section 0066. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both the WO document and McCarthy because they both read on the applicability of measuring TSP for the assessment of disease. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings the references that monitoring and evaluating the TSP markers are a must for diagnosing a diseases state and consequently establishing the proper cancer management and assessing the benefits of a particular treatment regimen.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. The provisional rejection of claims 241, 242, 244, 245, 248-250, 252, 253, 256, 265-316 and new claims 317-370 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 67 and 168-182 of copending Application No. 10/525,610 (filed March 24, 2006) is maintained.

Applicant notes they believe to sign a terminal disclaimer would be premature, see Remarks, page 37. This point of view has been considered, but found to be unpersuasive.

The rejection is maintained because Applicant's argument is not significant and the inventions are not patentably distinct from each other. The claims of both applications share the active method step of measuring an individual's plasma level of thrombospondin fragment or fragments with a binding agent in order to detect the presence and/or clinical course of a neoplastic disease and the copending application includes claims reading on a kit. The kit has no patentable weight and the said kit encompasses the claimed method measuring an individual's plasma level of thrombospondin fragment or fragments with a binding

agent in order to detect the presence and/or clinical course of a neoplastic disease.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner

works a *flexible schedule*, however she can normally be reached between the hours of 7:30 am to 6:30 pm, Monday through Saturday.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
21 December 2009
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643